

IN THE SPECIFICATION:

Please amend paragraph number [0001] as follows:

[0001] This application is a divisional of application Serial No. 09/767,363, filed January 23, 2001, now ~~US~~ U.S. Patent 6,648,831, issued November 18, 2003, which is a continuation of application Serial No. 08/770,138, filed December 19, 1996, now U.S. Patent 6,306,098, issued December 23, 2001.

Please amend paragraph number [0005] as follows:

[0005] It has previously been shown, however, that non-invasive means may be used for determining cardiac output while still using principles embodied in the Fick Equation. That is, expired CO₂ ("pCO₂") levels can be monitored to estimate arterial CO₂ concentrations and a varied form of the Fick Equation can be applied to evaluate observed changes in pCO₂ to estimate cardiac output. One use of the Fick Equation to determine cardiac output in non-invasive procedures requires the comparison of a "standard" ventilation event to a sudden change in ventilation which causes a change in expired CO₂ values and a change in excreted volume of CO₂. The commonly practiced means of providing a sudden change in effective ventilation is to cause the ventilated patient to ~~re-breath~~ re-breathe a specified amount of previously exhaled air. This technique has commonly been called "re-breathing."

Please amend paragraph number [0006] as follows:

[0006] Prior methods of re-breathing have used the partial pressure of end-tidal CO₂ to approximate arterial CO₂ while the lungs act as a tonometer to measure venous CO₂. That method of re-breathing has not proven to be a satisfactory means of measuring cardiac output because the patient is required to ~~breath~~ breathe directly into and from a closed volume in order to produce the necessary effect. However, it is usually impossible for sedated or unconscious patients to actively participate in inhaling and exhaling into a bag. The work of some researchers demonstrated that the Fick Equation could be further modified to eliminate the need to directly

calculate venous PCO_2 ($PVCO_2$) by assuming that the $PVCO_2$ does not change within the time period of the perturbation, an assumption that could be made by employing the partial re-breathing method. (See, Capek et al., "Noninvasive Measurement of Cardiac Output Using Partial CO_2 Rebreathing," *IEEE Transactions On Biomedical Engineering*, Vol. 35, No. 9, September 1988, pp. 653-661.)

Please amend paragraph number [0032] as follows:

[0032] In known re-breathing ventilation circuits 30, as shown in FIG. 2, the tubular portion 32 is inserted into the trachea of the patient by intubation procedures, and gas is provided to the patient from a ventilator machine (not shown) via an inspiratory hose 34 which is interconnected by a Y-piece 36 to an expiratory hose 38. An additional length of hose 40 is provided between the tubular portion 32 and the Y-piece 36 which acts as a deadspace for receiving exhaled gas. A three-way ~~valve 42~~ valve 42, generally positioned between the Y-piece 36 and the opening to the additional length of ~~hose 40~~ hose 40, is constructed for intermittent actuation to selectively direct the flow of gas. That is, at one setting, the valve 42 allows inspiratory gas to enter the tubular portion 32 while preventing movement of the gas into the additional length of hose 40. In a second setting, the valve 42 allows exhaled gas to enter into the expiratory hose 38 while preventing movement of gas into the additional length of hose 40. In a third setting, the three-way valve 42 directs exhaled air to enter into the additional length of hose 40 and causes the patient to ~~re-breathe~~ re-breathe the exhaled air on the following breath to thereby cause a change in effective ventilation.

Please amend paragraph number [0035] as follows:

[0035] The Y-piece 58 connects to an additional length of conduit or hose 60 which provides a deadspace for receiving exhaled gas from the patient. However, the additional length of hose 60 is structured to be selectively expandable to readily enable the volume of deadspace to be adjusted commensurate with the size or lung capacity of the patient, or to other ventilation

parameters, such as increased or decreased tidal volume or modified respiration rate. As suggested by the schematic drawing of FIG. 3, selective expansion of the deadspace may be accomplished by structuring the additional length of hose 60 with an expandable section 62 made of, for example, a piece of corrugated hose which can be lengthened or shortened by simply pulling or pushing the expandable section 62 along its longitudinal axis 64. The corrugated hose will retain the length at which it is positioned until adjusted again. Other suitable means of providing adjustable expansion of the volume of the deadspace are available, extending the length of the hose 60 being but one approach. A three-way valve 68 may be connected to the additional length of hose 60 to force inspiratory gas to enter the deadspace 70 upon inhalation. The three-way valve 68 is also structured to selectively prevent exhaled gas from entering the deadspace 70 during normal breathing or to direct exhaled gas into deadspace 70 during re-breathing episodes so that the patient is forced to ~~re-breath~~ re-breathe exhaled gas from the deadspace 70.

Please amend paragraph number [0045] as follows:

[0045] An adaptor fitting 134 may be used to connect a ventilation circuit 136 of a type previously described to the TGI apparatus 120. That is, a ventilation circuit 136 comprising a Y-piece 58 from which extends an inspiratory hose 54 and an expiratory hose 56 is structured with a flow meter line (not shown) attachable to a flow meter 72 (~~not shown~~) and a CO₂ sensor 74 for collecting data derived during a re-breathing event. In the illustrated TGI apparatus 120, the endotracheal tube 122 provides deadspace required for re-breathing in addition to the ventilation circuit 136 as previously described. To act as a deadspace, however, the TGI apparatus (i.e., the gas source 128 and flow meter 132) must be turned off, reduced or otherwise disabled. Exhaled air is thereby allowed to fill the endotracheal tube 122 and enter through the Y-piece 58. The endotracheal tube 122 and ventilation circuit 136 serve as deadspace when the TGI apparatus 120 is turned off. The volume of deadspace provided by the TGI apparatus configuration may be further increased or decreased, as necessary, by varying the depth to which the catheter 126 is positioned in the patient's trachea.

Please amend paragraph number [0050] as follows:

[0050] Perfused alveoli 160 and unperfused alveoli 162 are illustrated in FIG. 10. The perfused alveoli 160 are contacted with blood flowing through minute capillaries 164 surrounding the alveoli 160, 162 the venous blood 166 flowing toward the alveoli 160 and the arterial blood 168 flowing away from the alveoli 160 in the direction of arrow 170. In the alveoli 160, 162 a volume of gas known as the functional residual capacity (FRC) 176 remains following exhalation. A portion 172 of the alveoli 160, 162 which is evacuated upon exhalation (i.e., is ventilated) is representational of alveolar CO_2 ~~$(P_{\text{ACO}_2}) - (P_{\text{A}}\text{CO}_2)$~~ . In unperfused alveoli 162, the FRC 176 contains gas which is not evacuated during a breath, and the ventilated portion 178 of the alveoli 162 forms a space containing gas or CO_2 which is ventilated but not perfused. It is the ventilated portion 178 existing in the unperfused alveoli 162 which comprises parallel deadspace (PDS), so called because it is ventilated in parallel with the perfused alveoli.

Please amend paragraph number [0052] as follows:

[0052] Compensation is also made for parallel deadspace (See FIG. 10). Parallel deadspace CO_2 concentration is calculated as a low-pass filtered version of the mixed inspired CO_2 plus the airway deadspace times the previous end-tidal CO_2 concentration. The average $\text{CO}_{2\text{PDS}}$ is etCO_2 times airway deadspace plus inspired CO_2 volume divided by the tidal volume. Breath-by-breath calculation of parallel deadspace, or unperfused space, concentration is therefore:

$$\text{PDS}_{\text{CO}_2}(n) = \{[\text{FRC}/(\text{FRC} + V_t)] \times \text{PDS}_{\text{CO}_2}(n-1)\} + \\ (\{[V_i\text{CO}_2 + (\text{deadspace} \times \text{etCO}_2(n-1))/V_t] - \text{etCO}_2(n-1)]/V_t\} \times [V_t/(V_t + \text{FRC})]),$$

where V_t is the tidal volume (the volume of the breath), PDS is parallel deadspace (i.e., space in the lung that is ventilated but not perfused by blood flow), etCO_2 is the concentration of CO_2 at the end of the exhaled breath, or “end-tidal,” “deadspace” is the volume in the trachea and

bronchi through which air must pass to get to the alveoli but in which no gas exchange occurs (also defined as “serial deadspace,” See FIG. 10) and (n-1) indicates the previous breath.

Please amend paragraph number [0053] as follows:

[0053] Alveolar CO₂ partial pressure (~~“PACO₂”~~) (“P_ACO₂”) is calculated from the end-tidal CO₂ and the CO₂ in the parallel deadspace. Thus, if

$$etCO_2 = r \times \cancel{PACO_2} - \cancel{(P_ACO_2)} + (1-r) \cancel{PDS_{CO_2}} \underline{PDS_{CO_2}},$$

then

$$\cancel{PACO_2} - \cancel{(P_ACO_2)} = [etCO_2 - (1 - r) \times \cancel{PDS_{CO_2}} \underline{PDS_{CO_2}}] / r,$$

where r is the perfusion ratio calculated as the ratio of perfused alveolar ventilation divided by total alveolar ventilation, or (V_A - V_{PDS})/V_A. The perfusion ratio r is estimated to be about 0.92. Perfusion ratio can also be estimated by direct analysis of arterial blood.

Please amend paragraph number [0054] as follows:

[0054] The ~~PACO₂~~ (P_ACO₂) signal is then converted to CO₂ content using the following equation:

$$\underline{C_{CO_2}} = (6.957 \times Hb + 94.864) \times \ln(1 + 0.1933(\underline{P_{CO_2}} \underline{P_{CO_2}})),$$

where CCO₂ is the concentration of CO₂ and Hb is hemoglobin concentration. In some instances, a hemoglobin count may be readily available and is used in the equation. If hemoglobin (Hb) concentration is not available, the value of 11.0 is used in the software program.

Please amend paragraph number [0055] as follows:

[0055] Baseline values of etCO₂ and VCO₂, also referred to herein as “before CO₂ and before VCO₂,” are those values which exist during normal breathing and are calculated as the average of all samples between 27 and 0 seconds before the start of re-breathing. Once a re-breathing episode begins, the VCO₂ value during re-breathing, also referred to herein as

“during $\dot{V}CO_2$,” is calculated as the average $\dot{V}CO_2$ between 25 and 30 seconds of re-breathing.

The calculation of $\dot{C}CO_2$ during a re-breathing episode is determined using a regression line to predict the stable concentration of alveolar CO_2 ($\dot{C}CO_2$). To predict the $\dot{C}CO_2$ at which the signal will be stable (i.e., unchanging), the $\dot{C}CO_2$ is plotted versus the breath-to-breath change in concentration. The line is regressed and the intersection between the $\dot{C}CO_2$ and zero

$\Delta \dot{C}CO_2$ is the predicted stable point.